REMARKS

New claims 44-75 are pending in this application. Claims 1-43 have been cancelled. Applicants reserve the right to prosecute the subject matter of any of the cancelled claims in one or more related applications. Support for the new claims may be found in the specification. Specifically, example of support for claims 44-50 can be found on page 5, lines 6-18 and page 12, line 26 to page 13, line 16 of the instant specification. Support for claims 51-53 can be found on page 7, lines 21-25, page 30, lines 24-27, page 31, lines 10-23, and Figure 2C of the instant specification. Support for claim 54 can be found on page 29, lines 19-21 and page 31, lines 10-14 of the instant specification. Support for claims 55-60 can be found on page 4, lines 1-9 and original claim 12 of the instant specification. Support for claims 61-68 can be found on page 6, lines 17-22, page 30, lines 1-4 and 24-27, and Figures 4A and 5 of the instant specification. Support for claims 69 can be found on page 5, lines 15-18 and page 6, lines 17-22 of the instant specification. Support for claims 70-72 can be found on page 6, lines 17-22, page 7, lines 21-25, page 30, lines 24-27, page 31, lines 10-23, and Figure 2C of the instant specification. Support for claims 73-74 can be found on page 6, lines 17-22 of the instant specification. Support for claim 75 can be found on page 4, lines 10-14 of the instant specification. Thus, the new claims are fully supported by the instant specification and no new matter has been introduced.

Priority

The Examiner has denied Applicants priority to U.S. provisional patent application 60/260,080 filed January 6, 2001 (hereafter "the '080 application"). Allegedly the '080 application was filed with an incomplete Figure 6 such that the last 13,426 nucleotides of the genomic IKAP gene displaying the FD1 and FD2 mutations (SEQ ID NO:1) were missing. Applicants contend that a complete Figure 6 was filed showing all

66,476 nucleotides of SEQ ID NO:1. However, in effort to forward prosecution, Applicants have cancelled claims 1-43 in favor of new claims 44-75 which are fully described by the '080 application.

Support for claims 44-50 can be found on page 3, lines 3-11, page 6, lines 1-8, and page 14, lines 8-15 of the '080 application. Please note that the FD1 and FD2 mutations are contained within the portion of SEQ ID NO:1 that was undisputedly filed in the '080 application (i.e., residues 1-53,050). Furthermore, the '080 application identifies that these mutations are FD1 and FD2 which the '080 application also discloses are located within the IKAP gene.

Support for claims 51-53 can be found on page 6, lines 1-5, page 13, lines 3-16, and Figure 2C of the '080 application. Although the borders of exon 20 are not explicitly recited in the '080 application, it can be deduced using only the disclosed information. First, exon 20 is shown to be 74 nucleotides by Figure 5. RT-PCR on neuronal tissue from an FD patient using primers 19F and 23F yielded a 319 bp band. Wild type cDNA yields a 393 bp band when the same primers are used for RT-PCR. Because the '080 application discloses that the consequence of an FD1 mutation is the skipping of exon 20 (see page 6, lines 3-5 of the '080 application), one skilled in the art would realize that exon 20 is 74 bp (393-319). Secondly, the '080 application discloses that the FD1 mutation is a T to C change at residue 6 of intron 20 (see page 2, lines 27-28 of the '080 application). Figure 1 shows that intron 20 is 3' to exon 20. Thus exon 20 ends 6 residues previous to the FD1 mutation. Once exon 20 is identified on the IKAP genomic sequence given in Figure 6, the corresponding sequence could be identified on the IKAP cDNA. Using this information, one skilled in the art could identify that exon 20 is between 2,441 and 2,514 of the IKAP cDNA.

Additionally, the nucleic acid sequence of the exon 19/21 junction is evident in Figure 2C by reading the sequencing gel shown for the IKAP cDNA of an FD patient.

Accordingly, because the precise exon 19/21 border is shown, the nucleotides on either side of it are easily deduced.

Support for claim 54 can be found on page 2, lines 28-31 and page 6, lines 5-8 and page 11, lines 13-15 of the '080 application.

Support for claims 55-60 can be found on page 3, lines 15-24, page 13, line 28 to page 14, line 4 of the '080 application.

Support for claims 61-68 can be found on page 3, lines 12-14, page 9, lines 11-16, page 11, lines 23-27, page 12, lines 17-20, and page 13, line 28 to page 14, line 4 of the '080 application.

Support for claims 69 can be found on page 3, lines 12-14, and page 13, line 28 to page 14, line 4 of the '080 application. Please note that SEQ ID NOS:85 and 86 are oligonucleotide probes that span the FD1 and FD2 mutations, respectively. The '080 application discloses where the mutations are located in the IKAP gene (see page 2, lines 27-31 of the '080 application). The nucleic acid sequence surrounding the mutations is therefore disclosed in Figure 6 which itself discloses the FD1 and FD2 mutations and which are contained within the portion of SEQ ID NO:1 that was undisputedly filed in the '080 application.

Support for claims 70-72 can be found on page 3, lines 12-14, page 6, lines 1-5, page 13, lines 3-16, and Figure 2C of the '080 application. Please see explanation of support for claims 58-60 above.

Support for claims 73-74 can be found on page 3, lines 12-14 and page 15, lines 1-4 of the '080 application.

Support for claim 75 can be found on page 2, lines 28-31 and page 3, lines 15-24 of the '080 application.

For the reasons discussed above, Applicants request that the Examiner acknowledge that the presently pending claims are entitled to claim priority to the '080 application.

Claim Objections

The claims have been objected to for failure to include SEQ ID NOs. New claims 44-75 include SEQ ID NOs where applicable.

Rejections Under 35 U.S.C. §112

Claims 12-14 and 29-35 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants traverse this ground of rejection. In addition, new claims 44-75 distinctly claim Applicant's invention and are not indefinite.

Claim 43 has been rejected under 35 U.S.C. §112, first paragraph as allegedly not being enabled by the specification. Applicants traverse this ground of rejection. In addition, new claims 44-75 are enabled by the specification. In particular, oligonucleotides encompassed by the new claims detect mutations FD1 and FD2 in the IKAP gene.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112 is respectfully requested.

Rejections Under 35 U.S.C. §102

Claim 43 has been rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent Publication 2002/0168656 by Rubin et al. ("Rubin") and Anderson et al., 2001,

Am. J. Hum. Genetics 68:753-8 ("Anderson"). Rubin was filed January 16, 2002. Anderson published in March 2001.

Claims 1 and 43 have been rejected under 35 U.S.C. §102(b) as being anticipated by Slaugenhaupt et al., 2001, Am. J. Hum. Genetics 68:598-605 ("Slaugenhaupt") and Genbank Accession No. AF153419. Slaugenhaupt published in March 2001. Genbank Accession No. AF153419 published in February 2001.

Applicants contend that the presently claims are entitled to the benefit of priority to the '080 application. Thus, the effective filing date for the presently pending claims is January 6, 2001. As such none of the above-identified cited art constitutes prior art and can therefore not anticipate the present claims under §102(b).

Reconsideration and withdrawal of these §102 rejections is respectfully requested.

Claim 43 has been rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent 5,891,719 by Cohen et al. ("Cohen"). The Examiner alleges that Cohen teaches an isolated nucleic acid encoding IKAP that could be used to detect the FD2 mutation. Applicants respectfully disagree.

Claims 1 and 43 have rejected under 35 U.S.C. §102(b) as being anticipated by Genbank Accession No. AF153419 by Gill et al. ("Gill"). The Examiner contends that Gill teaches the IKAP cDNA that is disclose as SEQ ID NO:2 in the instant application and alleges that the nucleic acid molecule could be used to detect the FD2 mutation. Applicants respectfully disagree.

The nucleic acid molecule disclosed in Cohen and Gill is a wild type IKAP cDNA. The Examiner acknowledges that both Cohen and Gill teach a guanine residue at position 2,397 of the IKAP cDNA (in Cohen, the nucleic acid reside at position 2,087

corresponds to position 2,397 of SEQ ID NO:2 of the instant application). Applicants have disclosed that the IKAP cDNA associated with the FD2 mutation has a guanine to cytosine alteration at position 2,397.

Applicants were the first to discover and disclose that the IKAP gene was the gene mutated in Familial Dysautonomia as well as the location and identity of the particular FD1 and FD2 mutations. Without this information, one skilled in the art would not have known to use the IKAP cDNA to detect Familial Dysautonomia or where the FD2 mutation is located in the IKAP cDNA. Additionally, because the FD1 mutation is located in intron 20 of the IKAP gene, it is not present in the IKAP cDNA. Therefore disclosure of wild type IKAP cDNA as in Cohen and Gill could not have possibly disclosed detection of the FD1 mutation.

Anticipation under 35 U.S.C. § 102 requires that a single prior art publication disclose each and every element of the claimed invention, either expressly or inherently. See In re Robertson, 169 F.3d 743, 745, 49 U.S.P.Q. 2d 1949, 1950 (Fed. Cir. 1999). Absence from a cited reference of any element of a claim of a patent negates anticipation of that claim by that reference. Atlas Powder Co. v. E.I. Dupont de Nemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984). Neither Cohen nor Gill discloses each and every element of the pending claims. Specifically, there is no appreciation of the involvement of IKAP in Familial Dysautonomia or the identification or location of either of the FD1 or FD2 mutations and as such, could not have been used to detect the disorder.

For the above reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. §102 is respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claims 29, 30, 34, and 35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Cohen in view of U.S. Patent 5,968,740 by Fodor et al. ("Fodor"). Claims 29, 30, 34, and 35 have also been rejected under 35 U.S.C. §103(a) as being unpatentable over Gill in view of Cohen and further in view of Fodor. The Examiner alleges that it would have been obvious for one skilled in the art to package reagents for performing DNA detection assays involving the IKAP cDNA of Gill or Cohen in kits according to Fodor. Applicants respectfully disagree.

Although no longer pending, claims 29, 30, 34, and 35 were directed to kits for assaying the presence of a Familial Dysautonomia mutation. Currently pending claims 61-74 claim such kits. Claims 61-68 require primers specifically capable of amplifying a region of IKAP comprising either the FD1 or FD2 mutation. Claim 69 require a probe that detects the FD1 or FD2 mutation. Claims 70-72 require a probe which detects a deletion of exon 20 of IKAP. All of the presently claimed kits require specific reagents capable of detecting either the FD1 or FD2 mutations located in the IKAP genomic or cDNA. Additionally, claims 70-72 require a reagent designed based on the consequence of the FD1 mutation as exon 20 skipping. Applicants were the first to discover and disclose all of the required information necessary to make the novel and unobvious reagents in the claimed kits.

The wild type cDNA in Gill or Cohen does not connect IKAP to Familial Dysautonomia or disclose the location or identity of any of the mutations that cause Familial Dysautonomia. These deficiencies are not cured by Fodor. Fodor reports a methodology that can be used to identify a particular base in a nucleic acid by hybridization. Without the Applicants' disclosure, one skilled in the art would not know what two bases of the IKAP gene (out of the 5,924 bases of the cDNA or the 66,476 bases of the genomic DNA) to look at to assay for the presence of Familial Dysautonomia.

Claims 10-14 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gill in view of Cohen. The Examiner alleges it would have been obvious to clone the cDNA of Gill into a vector of Cohen and express the cDNA in a host cell of Cohen. Applicants respectfully disagree.

Although no longer pending, claims 10-14 were directed to vectors comprising a genomic or cDNA IKAP nucleic acid molecule (either wild type or mutant) and methods of producing the same. Currently pending claims 55-60 encompass vectors and host cells comprising the claimed nucleic acid molecules of the invention and claim 75 is directed to a method of producing a mutant IKAP polypeptide from mutant cDNA.

All of the claimed nucleic acid molecules require that either a FD1 and/or FD2 mutation be present in the nucleic acid molecule or that the nucleic acid molecule represents exon 19 directly connected to exon 21. In either case, Applicants were the first to discover each of the types of mutations in connection with IKAP. As such, merely a disclosure of a wild type cDNA in a vector or host cell does not disclose any of the claimed nucleic acids or vectors and host cells comprising the same.

Additionally, methods of producing a mutant IKAP polypeptide from mutant cDNA are encompassed by the claimed methods. Neither Gill nor Cohen report the FD2 mutation and as such could not have reported making the mutant polypeptide.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Graham v. Deere, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be

successful. In re O'Farrell, 853 F.2d 894, 902-4 (Fed. Cir. 1988); In re Vaeck, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. In re Dow Chemical Co., 5 U.S.P.Q. 2d 1529 (Fed. Cir. 1988). Here, the cited art fails on both counts - - none of the references suggest the invention therefore there can be no expectation of success.

For the reasons discussed above, Applicants respectfully request reconsideration and withdrawal of the rejection under §103.

Claims 10-14 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Slaugenhaupt in view of Cohen or Genbank Accession No. AF153419 in view of Cohen.

Claims 29, 30, 34, and 35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Rubin, Anderson, Slaugenhaupt, or Genbank Accession No. AF153419, each in view of Fodor.

The presently pending claims are entitled to the benefit of priority to the '080 application and thus have an effective filing date of January 6, 2001. Because this date is before the publication of any of Rubin, Anderson, Slaugenhaupt, and Genbank Accession No. AF153419, the references are not prior art and thus cannot be the basis of a rejection under §103(a).

For the above reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. §103 is respectfully requested.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

AUTHORIZATION

The Commissioner is hereby authorized to charge any fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 1829-4004US1.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

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Melissa B. Wenk / Kenneth H. Sonnenfeld
Reg. No. 53,759 / 33,285

Correspondence Address:
Morgan & Finnegan, L.L.P.
3 World Financial Center
New York, New York 10281-2101
(212) 415-8700 Telephone
(212) 415-8701 Facsimile

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